


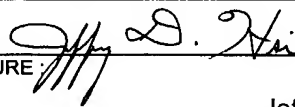


SUBSTITUTE FORM PTO-1390 U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		<b>ATTORNEY'S DOCKET NUMBER</b> 13596-003US1									
<b>TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371</b>		<b>U.S. APPLICATION NO. (If Known, see 37 CFR 1.5)</b> 10/088339									
INTERNATIONAL APPLICATION NO. PCT/GB00/03490	INTERNATIONAL FILING DATE 12 September 2000	PRIORITY DATE CLAIMED 16 September 1999									
TITLE OF INVENTION MEDICAMENTS CONTAINING PANTOTHENIC ACID											
APPLICANT(S) FOR DO/EO/US Paul Sherwood and David Keith Davies											
Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:											
1. <input type="checkbox"/> This is a <b>FIRST</b> submission of items concerning a filing under 35 U.S.C. 371. 2. <input type="checkbox"/> This is a <b>SECOND</b> or <b>SUBSEQUENT</b> submission of items concerning a filing under 35 U.S.C. 371. 3. <input type="checkbox"/> This is an express request to promptly begin national examination procedures (35 U.S.C. 371(f)). 4. <input type="checkbox"/> The US has been elected by the expiration of 19 months from the priority date (PCT Article 31). 5. <input checked="" type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371(c)(2)) a. <input checked="" type="checkbox"/> is attached hereto (required only if not communicated by the International Bureau). b. <input type="checkbox"/> has been communicated by the International Bureau. c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US). 6. <input type="checkbox"/> An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)). 7. <input type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)) a. <input type="checkbox"/> are attached hereto (required only if not communicated by the International Bureau). b. <input type="checkbox"/> have been communicated by the International Bureau. c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired. d. <input type="checkbox"/> have not been made and will not be made. 8. <input type="checkbox"/> An English language translation of amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)). 9. <input type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). 10. <input type="checkbox"/> An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).											
<b>Items 11 to 16 below concern other documents or information included:</b>											
11. <input type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98. 12. <input type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included. 13. <input checked="" type="checkbox"/> A <b>FIRST</b> preliminary amendment. <input type="checkbox"/> A <b>SECOND</b> or <b>SUBSEQUENT</b> preliminary amendment. 14. <input type="checkbox"/> A substitute specification. 15. <input type="checkbox"/> A change of power of attorney and/or address letter. 16. <input type="checkbox"/> Other items or information: <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/> <input type="checkbox"/>											
<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td colspan="2" style="padding: 2px;"><b>CERTIFICATE OF MAILING BY EXPRESS MAIL</b></td> <td style="padding: 2px;">Express Mail Label No. <u>EL940866708US</u></td> </tr> <tr> <td colspan="3" style="padding: 5px;">           I hereby certify under 37 CFR §1.10 that this correspondence is being deposited with the United States Postal Service as Express Mail Post Office to Addressee with sufficient postage on the date indicated below and is addressed to the Commissioner for Patents, Washington, DC 20231.         </td> </tr> <tr> <td style="padding: 5px; text-align: center;"> <u>3-15-02</u>            Date of Deposit         </td> <td style="padding: 5px; text-align: center;">             Signature         </td> <td style="padding: 5px; text-align: center;"> <u>Henry Jenkins</u>            Typed Name of Person Signing         </td> </tr> </table>			<b>CERTIFICATE OF MAILING BY EXPRESS MAIL</b>		Express Mail Label No. <u>EL940866708US</u>	I hereby certify under 37 CFR §1.10 that this correspondence is being deposited with the United States Postal Service as Express Mail Post Office to Addressee with sufficient postage on the date indicated below and is addressed to the Commissioner for Patents, Washington, DC 20231.			<u>3-15-02</u> Date of Deposit	 Signature	<u>Henry Jenkins</u> Typed Name of Person Signing
<b>CERTIFICATE OF MAILING BY EXPRESS MAIL</b>		Express Mail Label No. <u>EL940866708US</u>									
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<u>3-15-02</u> Date of Deposit	 Signature	<u>Henry Jenkins</u> Typed Name of Person Signing									

IC10 Rec'd PCT/PTO 15 MAR 2002

U.S. APPLICATION NO. (IF KNOWN) <b>10/088339</b>		INTERNATIONAL APPLICATION NO. PCT/GB00/03490		ATTORNEY'S DOCKET NUMBER <b>13596-003US1</b>	
17. <input checked="" type="checkbox"/> The following fees are submitted:  <b>Basic National Fee ( 37 CFR 1.492(a)(1)-(5) ):</b>  Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO..... <b>\$1040</b>  International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO ..... <b>\$890</b>  International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO..... <b>\$740</b>  International preliminary examination fee paid to USPTO (37 CFR 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4)..... <b>\$710</b>  International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4)..... <b>\$100</b>  <div style="text-align: right;"><b>ENTER APPROPRIATE BASIC FEE AMOUNT =</b></div>				<b>CALCULATIONS PTO USE ONLY</b>	
Surcharge of <b>\$130</b> for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(e)).				\$0.00	
Claims	Number Filed	Number Extra	Rate		
Total Claims	14 - 20 =	0	x \$18	\$0.00	
Independent Claims	1 - 3 =	0	x \$84	\$0.00	
MULTIPLE DEPENDENT CLAIMS(S) (if applicable)			+ \$280	\$0.00	
<b>TOTAL OF ABOVE CALCULATIONS =</b>				\$890.00	
<input checked="" type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2.				\$445.00	
<b>SUBTOTAL =</b>				\$445.00	
Processing fee of <b>\$130</b> for furnishing the English Translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(f))				\$0.00	
<b>TOTAL NATIONAL FEE =</b>				\$445.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). <b>\$40.00</b> per property +				\$0.00	
<b>TOTAL FEES ENCLOSED =</b>				\$445.00	
				<b>Amount to be refunded:</b>	\$
				<b>Charged:</b>	\$
a. <input checked="" type="checkbox"/> A check in the amount of \$445.00 to cover the above fees is enclosed. b. <input type="checkbox"/> Please charge my Deposit Account No. 06-1050 in the amount of \$0.00 to cover the above fees. A duplicate copy of this sheet is enclosed. c. <input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 06-1050. A duplicate copy of this sheet is enclosed.					
<b>NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b) must be filed and granted to restore the application to pending status.</b>					
SEND ALL CORRESPONDENCE TO:					
Jeffrey D. Hsi FISH & RICHARDSON P.C. 225 Franklin Street Boston, Massachusetts 02110-2804 (617) 542-5070 phone (617) 542-8906 facsimile			 SIGNATURE		
			NAME Jeffrey D. Hsi		
			REGISTRATION NUMBER 40,024		

10/088339

1610 Rec'd PCT/PTO 15 MAR 2002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Paul Sherwood, et al  
 Serial No. : Unassigned  
 Filed : Herewith  
 Title : MEDICAMENTS CONTAINING PANTOTHENIC ACID

**BOX PCT**

Commissioner for Patents  
 Washington, D.C. 20231

PRELIMINARY AMENDMENT

Prior to examination, please amend the application as follows:

In the specification:

Replace the title beginning at page 1, line 1, with the following rewritten title:

**--MEDICAMENTS CONTAINING PANTOTHENIC ACID--**

Insert the following heading at page 1, between lines 1 and 2, before the first paragraph:

**--TECHNICAL FIELD--**

Insert the following heading at page 1, between lines 3 and 4, before the second paragraph:

**--BACKGROUND--**

Insert the following heading at page 1, between lines 8 and 9, before the fourth paragraph:

**--DETAILED DESCRIPTION--**

CERTIFICATE OF MAILING BY EXPRESS MAIL

Express Mail Label No. EL940866708US

I hereby certify under 37 CFR §1.10 that this correspondence is being deposited with the United States Postal Service as Express Mail Post Office to Addressee with sufficient postage on the date indicated below and is addressed to the Commissioner for Patents, Washington, D.C. 20231.

Date of Deposit 3-15-02

Signature [Handwritten Signature]

Typed or Printed Name of Person Signing Certificate Leroy Jenkins

Attorney's Docket No.: 13596-003US1

--“An effective amount” refers to an amount of pantothenic acid or its derivative which confers a therapeutic effect on the treated subject. The therapeutic effect may be objective (i.e., measurable by some test or marker) or subjective (i.e., subject gives an indication of or feels an effect). A typical dose is about 2 mls of an aqueous solution of about 500 mg of the acid salt. The medicament is injected directly into the site of the inflamed joint. A program of injections is generally desirable in which dosages similar to that indicated above are given at intervals of a few days to about one week. Reduced inflammation and increased freedom of movement is usually noticeable after about a week from the initial injection.--

--All references cited herein, whether in print, electronic, computer readable storage media or other form, are expressly incorporated by reference in their entirety, including but not limited to, abstracts, articles, journals, publications, texts, treatises, internet web sites, databases, patents, and patent publications.--

## --OTHER EMBODIMENTS

All of the features disclosed in this specification may be combined in any combination. Thus, unless expressly stated otherwise, each feature disclosed is only an example of a generic series of equivalent or similar features.

It is to be understood that while the invention has been described in conjunction with the detailed description thereof, the foregoing description is intended to illustrate and not limit the scope of the invention, which is defined by the scope of the appended claims. Other aspects, advantages, and modifications are within the scope of the following claims.--

In the claims:

Cancel claims 1-9.

Add claims 10-24.

--10. (New) A method of alleviating pain in an inflamed or painful joint of a mammal, comprising administration of an effective amount of pantothenic acid or a derivative thereof by injection into the region of an inflamed or painful joint to obtain alleviation of said inflammation or pain.

11. (New) The method according to claim 10, in which the joint is affected by a disorder from tennis elbow, housemaid's knee, frozen shoulder, inflamed knee joints and hip and back pain associated with inflammation or restricted movement in the spinal vertebrae.

12. (New) The method according to claim 10, wherein the derivative is a salt of pantothenic acid.

13. (New) The method according to claim 12, wherein the salt is the calcium salt.

14. (New) The method according to claim 10, wherein the injectable medicament comprises an aqueous solution of pantothenic acid or a derivative thereof.

15. (New) The method according to claim 14, wherein the medicament is co-administered with a local anesthetic.

16. (New) The method according to claim 14, wherein the medicament is co-administered with cysteine or glucosamine.

- \_\_\_\_\_

Attorney's Docket No.: 13596-003US1

Claims 1-9 have been canceled. Claims 10-24 have been added.

Please apply any other charges or credits to Deposit Account No. 06-1050, referencing attorney docket no. 13596-003US1.

Date: March 15, 2002

Signature: \_\_\_\_\_

20404026.doc

Applicant : Paul Sherwood, et al  
Serial No. : Unassigned  
Filed : Herewith  
Page : 6

Attorney's Docket No.: 13596-003US1  
1003339-091003

**Version with markings to show changes made**

**In the specification:**

The title beginning at page 1, line 1, has been amended as follows:

**MEDICAMENTS CONTAINING [PANTHOTHENIC] PANTOTHENIC ACID**

Paragraph beginning at page 2, line 20, has been amended as follows:

"An effective amount" refers to an amount of pantothenic acid or its derivative which confers a therapeutic effect on the treated subject. The therapeutic effect may be objective (i.e., measurable by some test or marker) or subjective (i.e., subject gives an indication of or feels an effect). A typical dose is about 2 mls of an aqueous solution of about 500 mg of the acid salt. The medicament is injected directly into the site of the inflamed joint. A [programme] program of injections is generally desirable in which dosages similar to that indicated above are given at intervals of a few days to about one week. Reduced inflammation and increased freedom of movement is usually noticeable after about a week from the initial injection.

**In the claims:**

Claims 1-9 have been cancelled.

**MEDICAMENTS CONTAINING PANTHOTHENIC ACID**

This invention relates to medicaments and their use in the alleviation of inflammation and pain in joints.

Pain or loss of movement in joints is a common occurrence, particularly among the elderly or those who have suffered damage to cartilage, bone surfaces or ligaments.

Standard methods of treatment include the administration of corticosteroids by injection into the site of the inflammation. However, relief tends to be temporary and long term use carries a number of contraindications.

Pantothenic acid (sometimes known as vitamin B5) and its salts have been used as a dietary supplement and for treatment of bronchial asthma, hay-fever, sinusitis and neurodermatitis.

It has now been found that pantothenic acid is of value in reducing inflammation when injected into the region of an affected joint.

According to the present invention there is provided use of pantothenic acid or a derivative thereof in the preparation of a medicament for administration by injection into the region of a joint for alleviation of inflammation or pain.

The pantothenic acid may be used in the form of a salt, e.g. the calcium salt. Pantothenic acid is a naturally occurring substance in plant and animal tissue. A particularly rich source is royal jelly obtainable from honey bee colonies. It may be used in its naturally occurring state or as a chemically pure material. Synthetic methods of preparations include those described in US Patent Nos. 2,780,645; 2,845,456 and 2,934,428. The free acid and its salts are optionally active and the dextro-rotatory isomer is preferred.

Conveniently, a medicament is prepared by dissolving the active ingredient, i.e. pantothenic acid or a derivative in a suitable solvent, e.g. water, and injecting the solution into the affected joint. The initial treatment may cause some pain and it may, therefore, be desirable to co-administer a local anaesthetic, e.g. lignocaine, at the same time or shortly before the injection of the pantothenic acid.

Other physiologically active materials may be co-administered, e.g. cysteine or glucosamine.

It may also be desirable to co-administer within the same treatment regime, a surface active phospholipid (SAPL) such as dipalmitoyl-phosphatidyl choline (DPPC) or phosphatidyl glycerol (PG). Preferably, a mixture of DPPC and PG is employed. A preferred protein-free SAPL composition comprising a blend of DPPC and PG is available from Britannia Pharmaceuticals Ltd of Brighton Road, Redhill under the trade mark 'Alec'. SAPL's such as 'Alec' are believed to act as a lubricant in joints, taking over to some extent the function of synovial fluid.

The medicaments of this invention may be used in the treatment of several conditions associated with inflammation or reduced movement of joints. Examples include tennis elbow, housemaid's knee, frozen shoulder, inflamed knee joints and hips and back pain associated with inflammation or restricted movement in the spinal vertebrae.

A typical dose is about 2 mls of an aqueous solution of about 500 mg of the acid salt. The medicament is injected directly into the site of the inflamed joint. A programme of injections is generally desirable in which dosages similar to that indicated above are given at intervals of a few days to about one week. Reduced

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inflammation and increased freedom of movement is usually noticeable after about a week from the initial injection.

**CLAIMS:-**

1. Use of pantothenic acid or a derivative thereof in the preparation of a medicament for administration by injection into the region of a joint for alleviation of inflammation or pain.
2. Use according to claim 1 wherein the derivative is a salt of pantothenic acid.
3. Use according to claim 2 wherein the salt is the calcium salt.
4. Use according to any one of the preceding claims wherein the medicament comprises an aqueous solution of pantothenic acid or a derivative thereof.
5. Use according to any one of the preceding claims wherein the medicament includes a local anaesthetic.
6. Use according to any one of the preceding claims wherein the medicament is co-administered with cysteine or glucosamine.
7. Use according to any one of the preceding claims wherein the medicament is co-administered with a surface-active phospholipid (SAPL).
8. Use according to claim 7 wherein the SAPL comprises dipalmitoylphosphatidyl choline.
9. Use according to claim 7 or 8 wherein the SAPL comprises phosphatidyl glycerol.

## (12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
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22 March 2001 (22.03.2001)

PCT

(10) International Publication Number  
**WO 01/19359 A2**(51) International Patent Classification<sup>7</sup>: A61K 31/00[GB/GB]; 2 Devonshire Place, London W1N 2PA (GB).  
DAVIES, David, Keith [GB/GB]; 36 Harvest Bank Road,  
West Wickham, Kent BR4 9DJ (GB).

(21) International Application Number: PCT/GB00/03490

(22) International Filing Date:  
12 September 2000 (12.09.2000)(74) Agent: WOODCRAFT, David, Charles; Brookes &  
Martin, High Holborn House, 52-54 High Holborn, Lon-  
don WC1V 6SE (GB).

(25) Filing Language: English

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## Published:

(71) Applicant (*for all designated States except US*): BRI-  
TANNIA PHARMACEUTICALS LIMITED [GB/GB];  
41-51 Brighton Road, Redhill, Surrey RH1 6YS (GB).— Without international search report and to be republished  
upon receipt of that report.

(72) Inventors; and

*For two-letter codes and other abbreviations, refer to the "Guid-  
ance Notes on Codes and Abbreviations" appearing at the begin-  
ning of each regular issue of the PCT Gazette.*(75) Inventors/Applicants (*for US only*): SHERWOOD, Paul

WO 01/19359 A2

(54) Title: MEDICAMENTS CONTAINING PANTOTHENIC ACID

(57) Abstract: A medicament and procedure is disclosed for alleviation of inflammation or pain in the region of a human or animal joint. The procedure involves injecting pantothenic acid or a derivative thereof into the vicinity of the affected joint.

## COMBINED DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am an original, first and joint inventor of the subject matter which is claimed and for which a patent is sought on the invention entitled MEDICAMENTS CONTAINING PANTOTHENIC ACID, the specification of which was filed on March 15, 2002 as Application Serial No. 10/088,339 and was amended on March 15, 2002.

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose all information I know to be material to patentability in accordance with Title 37, Code of Federal Regulations, §1.56.

I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

Country	Application No.	Filing Date	Priority Claimed
WIPO	GB/00/03490	September 12, 2000	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Great Britain	9921985.9	September 16, 1999	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

I hereby appoint the following attorneys and/or agents to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:

Jeffrey D. Hsi, Reg. No. 40,024  
John F. Hayden, Reg. 37,640  
Y. Rocky Tsao, Reg. 34,053

Frank R. Occhiuti, Reg. 35,306  
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Address all correspondence to JEFFREY D. HSI at:

FISH & RICHARDSON P.C.  
225 Franklin Street  
Boston, Massachusetts 02110-2804

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

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Date: 2/9/02

10088339, 091002

Attorney's Docket No.: 13596-003US1

**Combined Declaration and Power of Attorney**

Page 2 of 2 Pages

2-00 Full Name of Inventor: DAVID KEITH DAVIES

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